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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,282	07/22/2002	Guy Krippner	150070.402USPC	8714

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/088,282	KRIPPNER ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-13,15-17,19-27 and 30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-13, 15-17, 19-27 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included amendment to claims 32 and 33, filed on 11/10/2006, is made of record. Claims 1, 2, 4-13, 15-17, 19-27 and 30-33 are pending. In view of applicants' amendment , the 112 first paragraph rejection made in the previous office action has been obviated. However, the following new grounds of rejections are applied to currently pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-13, 15-17, 19-23, 27 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description Rejection. Following apply.

Representative examples of structurally diverse compounds generically embraced in the invention bearing at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ are not shown to possess in vitro activity much less in vivo uses claimed herein. Instant compound with the above said formula can embrace compounds with substituents bearing plethora of structural cores and functional groups and other groups which include variously substituted monocyclic rings, bicyclic rings,

tricyclic rings , spiro with variable ring sizes and variable heteroatoms variety of reactive functional groups such COOH, OH ,SH, amido, sulfoxides, sulfones, nitrile, carbamates etc. There is no reasonable basis for assuming that the myriad of compounds embraced by the claim language will all share the same bioactivity profile since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive art such as the pharmaceuticals.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method of use. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, 1117, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The instant specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 116). The skilled artisan cannot envision what the detailed chemical structure of the encompassed genera of all ligands that would be capable binding to the capsid without any teaching in the specification two choose such ligands, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a suitable choices. The ligands themselves are required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, at 1483 (finding claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the bovine sequence). Therefore, only the ligands that bind to capsid, as taught by the instant specification, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. § 112, first paragraph.

Claims 27 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating and or diagnosis of human rhinoviral

infections with compounds positively recited in the specification, does not reasonably provide enablement for treating human rhinoviral infections with structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claims 27 and 31-33 are drawn to "treating and or diagnosis of a human rhinoviral infections". Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the HRV capsid binding property of exemplified instant compounds, claims 27 and 31-33 reach through diagnosis and treatment of human rhinoviral infections with structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of exemplified instant compounds as inhibitor of HRV, based on limited assay showing inhibition of HRV infection of lung provided in the specification (page 58), it is claimed that diagnosis and treatment of human rhinoviral infections with structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ in general, for which there is no enabling disclosure.

The instant compounds are disclosed to have HRV inhibitory activity due to capsid binding and it is recited that the instant compounds are useful in diagnosis and treatment of human rhinoviral infections with structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$, for which applicants provide no competent evidence. The fact that a single class of compounds can be used diagnosis and treatment of human rhinoviral infections with structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ are new finding for which there is no support in the prior art. Furthermore, the instant compounds are based on the capsid binding property modeled on HRV as evident from pages 1-6 of the specification. There is no evidence provided that would extrapolate such a property to diagnosis and treatment of human rhinoviral infections with any structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. In addition, the instant compounds, which are said to be derived from, the prior art compound, distinctly show different activities as indicated in page 26 (category A & B). Thus, there is no showing that the instant structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ would behave similarly.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Use of structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ in diagnosis and treatment of human rhinoviral infections with

2) The state of the prior art: A very recent publication expressed that the antiviral effects of HRV inhibitors are unpredictable. See Hayden , F. G., Review in Medical Virology, 14, 17-31, 2004, provided previously.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence any or all structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$ would behave similarly to those compounds exemplified. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of

unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no teaching or suggestion that all structurally diverse class of compounds mentioned above would be useful for treating and diagnosis of human rhinoviral infection and the state of the art is that the effects of such inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace large genus of compounds with structural diversity with no showing of their interaction with capsid.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed structurally diverse compounds towards treating and diagnosis of the said viral infections of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based

on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-13, 15-17, 19-26 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Judice et al., US 6,395,724.

Judice et al., teaches several multibinding inhibitors of cyclooxygenase-2, which include compounds, process of making and composition of instant structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column 2, formula 1 and note with the given definition of L, X, p and n, compounds, process of making and composition taught by Judice et al., include compounds, process of making and composition of instant structurally diverse class compounds with at least moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column

2-32 for various preferred embodiments and detail description of the invention. Particularly see column 33-104 for various specifically recited choices of L, X, p and n. See column 109-114 for examples and also see figures 3-18 for various compounds.

Instant claim 1 recites in the preamble "capable of binding to a picornavirus capsid... and at least two capsid binding moieties" but these are attributes to the said class of compounds with at least two units of $Ar^1(X)_mW(Y)_nAr^2$.

The attribute that a compound of known structure has does not alter its structure in any way. See Intirtool, LTD. V. Texar Corp., 70 USPQ2D 1780. Note court held that "In general, a claim preamble is limiting if recites essential structure or steps or if it is necessary to give" life, meaning, and vitality to claim.'.... However, if the body of the claim describes a structurally complete invention such that deletion of the preamble phrase does not effect the structure or steps of the claimed invention,' the preamble is generally not limiting unless there is clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art.""

Instant claim is a compound claim and is clearly defined by a structure namely at least two unit of $Ar^1(X)_mW(Y)_nAr^2$ core. Omission of the attributes to the compound of genus of claim 1 would not alter the structure of these compounds.

Hence, this rejection is applied.

Claims 1, 2, 4-13, 15-17, 19-26 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Marquess et al., US 6,420,354 et al..

Marquess et al., teaches several sodium channel modulating agents which include compounds, process of making and composition of instant structurally diverse

class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column 3, formula 1 and note with the given definition of L, X, p and n, compounds, process of making and composition taught by Marquess et al., include compounds, process of making and composition of instant structurally diverse class compounds with at least moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column 3-15 for various preferred embodiments and detail description of the invention. Particularly see column 27-90 for various specifically recited choices of L, X, p and n. See column 103-170 for examples 1-53 and also see sheets of figures 2-25 for various compounds.

Instant claim 1 recites in the preamble "capable of binding to a picornavirus capsid... and at least two capsid binding moieties" but these are attributes to the said class of compounds with at least two units of $Ar^1(X)_mW(Y)_nAr^2$.

The attribute that a compound of known structure has does not alter its structure in any way. See Intirtool, LTD. V. Texar Corp., 70 USPQ2D 1780. Note court held that "In general, a claim preamble is limiting if recites essential structure or steps or if it is necessary to give" life, meaning, and vitality to claim.'.... However, if the body of the claim describes a structurally complete invention such that deletion of the preamble phrase does not effect the structure or steps of the claimed invention,' the preamble is generally not limiting unless there is clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art.""

Instant claim is a compound claim and is clearly defined by a structure namely at least two unit of $Ar^1(X)_mW(Y)_nAr^2$ core. Omission of the attributes to the compound of

genus of claim 1 would not alter the structure of these compounds.

Hence, this rejection is applied.

Claims 1, 2, 4-13, 15-17, 19-26 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Numerof et al., US 6,420,354 et al..

Numerof et al., teaches several sodium channel modulating agents which include compounds, process of making and composition of instant structurally diverse class compounds with at least two capsid binding moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column 2, formula 1 and note with the given definition of L, X, p and n, compounds, process of making and composition taught by Numerof et al., include compounds, process of making and composition of instant structurally diverse class compounds with at least moieties selected from formula $Ar^1(X)_mW(Y)_nAr^2$. See column 2-25 for various preferred embodiments and detail description of the invention. Particularly see column 26-101 for various specifically recited choices of L, X, p and n. See column 104-116 for examples 1-14 and also see sheets of figures 1-12 for various compounds.

Instant claim 1 recites in the preamble "capable of binding to a picornavirus capsid... and at least two capsid binding moieties" but these are attributes to the said class of compounds with at least two units of $Ar^1(X)_mW(Y)_nAr^2$.

The attribute that a compound of known structure has does not alter its structure in any way. See Intirtool, LTD. V. Texar Corp., 70 USPQ2D 1780. Note court held that "In general, a claim preamble is limiting if recites essential structure or steps or if it is necessary to give" life, meaning, and vitality to claim.'.... However, if the body of the

claim describes a structurally complete invention such that deletion of the preamble phrase does not effect the structure or steps of the claimed invention,' the preamble is generally not limiting unless there is clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art.""

Instant claim is a compound claim and is clearly defined by a structure namely at least two unit of $Ar^1(X)_mW(Y)_nAr^2$ core. Omission of the attributes to the compound of genus of claim 1 would not alter the structure of these compounds.

Hence, this rejection is applied.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

2/3/2006